

CLAIM AMENDMENTS

Please amend the claims as follows:

Cancel claims 96-114 without prejudice or admission.

Amend claims 69, 75-80, 86-90 and 115-117, and add new claims 118-139 as set forth below:

69. (Once amended) An antibody that is capable of binding human CTLA4 with a binding affinity of about 10^8 M^{-1} or greater, which antibody comprises a heavy chain variable region [having a contiguous amino acid sequence encoded by] of a human V_H 3-30.3 or V_H 3-33 gene, [said human V_H 3-30.3 or V_H 3-33 gene having at least one mutation shown in Figure 6] and wherein the antibody inhibits binding of the human CTLA4 to B7-1 or to B7-2.

D,
70. An antibody according to claim 69, wherein said antibody binds human CTLA4 with a binding affinity of about 10^9 M^{-1} or greater.

71. An antibody according to claim 69, wherein said antibody does not bind CTLA4 from mouse.

72. An antibody according to claim 69, wherein said antibody binds CTLA4 from cynomolgus monkey.

73. An antibody according to claim 69, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about 1 μ g/mL.

74. An antibody according to claim 69, which antibody reduces binding of human CTLA4 to B7-2 by at least 50% when the concentration of antibody is at least about 1 μ g/mL.

D1
75. (Once amended) An antibody according to claim 69 wherein the [contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene] heavy chain variable region comprises [at least one] CDR amino acid [sequence selected from the group consisting of SEQ ID NOS:27-28, 32-34 and 37-39] sequences set forth in SEQ ID NOS:27, 32 and 37.

76. (Once amended) An antibody according to claim 69, wherein the [contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene] heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:17, 19 and 23.

77. (Once amended) An antibody according to claim 69, which antibody further comprises a light chain variable region [having a contiguous amino acid sequence encoded by] of a human V_K A-27 or V_K L-15 gene [, said human V_K A-27 or V_K L-15 gene having at least one mutation shown in Figure 5].

Serial No. 09/644,668
Second Preliminary Amendment

Docket No. 4280/1M321US1
Page 4 of 17

78. (Once amended) An antibody according to claim 77, wherein the [contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene] light chain variable region comprises [at least one] CDR amino acid [sequence selected from the group consisting of SEQ ID NOS:24-26, 29-31 and 35-36] sequences set forth in SEQ ID NOS:24, 29 and 35.

79. (Once amended) An antibody according to claim 77, wherein the [contiguous amino acid sequence encoded by the human V_K A-27 or V_K L-15 gene] light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:7, 9 and 13.

D1
80. (Once amended) An antibody that is capable of binding human CTLA4 with a binding affinity of about 10⁸ M⁻¹ or greater, which antibody comprises a light chain variable region [having a contiguous amino acid sequence encoded by] of a human V_K A-27 or V_K L-15 gene, [said human V_K A-27 or V_K L-15 gene having at least one mutation shown in Figure 5] and wherein the antibody inhibits binding of the human CTLA4 to B7-1 or to B7-2.

81. An antibody according to claim 80, wherein said antibody binds human CTLA4 with a binding affinity of about 10⁹ M⁻¹ or greater.

82. An antibody according to claim 80, wherein said antibody does not bind CTLA4 from mouse.

83. An antibody according to claim 80, wherein said antibody binds CTLA4 from cynomolgus monkey.

84. An antibody according to claim 80, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about 1 μ g/mL.

D1
85. An antibody according to claim 80, which antibody reduces binding of human CTLA4 to B7-2 by at least 50% when the concentration of antibody is at least about 1 μ g/mL.

86. (Once amended) An antibody according to claim 80, wherein the [contiguous amino acid sequence encoded by the human V_k A-27 or V_k L-15 gene] light chain variable region comprises [at least one] CDR amino acid [sequence selected from the group consisting of SEQ ID NOS:24-26, 29-31 and 35-36] sequences set forth in SEQ ID NOS:24, 29 and 35.

87. (Once amended) An antibody according to claim 80, wherein the [contiguous amino acid sequence encoded by the human V_k A-27 or V_k L-15 gene] light

chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:7, 9 and 13.

88. (Once amended) An antibody according to claim 80, which antibody further comprises a heavy chain variable region [having a contiguous amino acid sequence encoded by] of a human V_H 3-30.3 or V_H 3-33 gene [, said human V_H 3-30.3 or V_H 3-33 gene having at least one mutation shown in Figure 6].

D1
89. (Once amended) An antibody according to claim 88, wherein the [contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene]
heavy chain variable region comprises [at least one] CDR amino acid [sequence selected from the group consisting of SEQ ID NOS:27-28, 32-34 and 37-39] sequences set forth in SEQ ID NOS:27, 32 and 37.

90. (Once amended) An antibody according to claim 88, wherein the [contiguous amino acid sequence encoded by the human V_H 3-30.3 or V_H 3-33 gene]
heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOS:17, 19 and 23.

91. (Once amended) A human antibody that:

(a) binds human CTLA4 with a binding affinity of about [10⁹] 10⁸ M⁻¹ or greater;

(b) inhibits binding of the human CTLA4 to B7-1 or B7-2; and

Serial No. 09/644,668
Second Preliminary Amendment

Docket No. 4280/1M321US1
Page 7 of 17

{M:\4280\1m321us1\00007746.DOC [REDACTED]}

(c) does not cross-react with non-lymphoid tissue.

92. An antibody according to claim 91 that does not bind CTLA4 from mouse.

93. An antibody according to claim 91, wherein said antibody binds CTLA4 from cynomolgus monkey.

94. An antibody according to claim 91, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about 1 μ g/mL.

D1
95. An antibody according to claim 91, which antibody reduces binding of human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least about 1 μ g/mL.

96 – 114. (Cancelled)

115. (Once amended) An antibody comprising:

- (a) a heavy chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NOS:19; and
- (b) a light chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NO:9,

wherein the antibody is capable of binding CTLA-4.

Serial No. 09/644,668
Second Preliminary Amendment

Docket No. 4280/1M321US1
Page 8 of 17

116. (Once amended) An antibody comprising:

- (a) a heavy chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NOS:17; and
- (b) a light chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NO:7,

wherein the antibody is capable of binding CTLA4.

D 1
117. (Once amended) An antibody comprising:

- (a) a heavy chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NOS:23; and
- (b) a light chain variable amino acid sequence having the amino acid sequence set forth in SEQ ID NO:13,

wherein the antibody is capable of binding CTLA4.

118. (New) An antibody capable of binding CTLA4, which antibody comprises:

- (a) a heavy chain variable region having CDR sequences set forth in SEQ ID NOS:27, 32 and 37; and
- (b) a light chain variable region having CDR sequences set forth in SEQ ID NOS:24, 29 and 35.

119. (New) An antibody capable of binding CTLA4, which antibody comprises:

- (a) a heavy chain variable region having CDR sequences set forth in SEQ ID NOS:27, 33 and 37; and
- (b) a light chain variable region having CDR sequences set forth in SEQ ID NOS:25, 30 and 35.

120. (New) An antibody capable of binding CTLA4, which antibody comprises:

- (a) a heavy chain variable region having CDR sequences set forth in SEQ ID NOS:28, 34 and 38; and
- (b) a light chain variable region having CDR sequences set forth in SEQ ID NOS:26, 31 and 36.

121. (New) An antibody capable of binding human CTLA4, which antibody comprises:

- (a) a heavy chain variable region of a human V_H 3-30.3 gene; and
- (b) a light chain variable region of a human V_K A-27 gene.

122. (New) An antibody according to claim 121, wherein the antibody is capable of binding human CTLA4 with a binding affinity of about 10⁸ M⁻¹ or greater.

123. (New) An antibody according to claim 121, wherein the antibody is capable of binding human CTLA4 with a binding affinity of about 10⁸ M⁻¹ or greater.

124. (New) An antibody according to claim 121, wherein the antibody inhibits binding of the human CTLA4 to B7-1 or to B7-2.

125. (New) An antibody according to claim 124, wherein the antibody reduces binding of the human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least 1 μ g/mL.

126. (New) An antibody according to claim 124, wherein the antibody reduces binding of the human CTLA4 to B7-2 by at least 50% when the concentration of antibody is at least 1 μ g/mL.

D1
127. (New) An antibody according to claim 121, wherein the antibody does not cross-react with non-lymphoid tissue.

128. (New) An antibody according to claim 121, wherein the antibody does not bind CTLA4 from mouse.

129. (New) An antibody according to claim 121, wherein the antibody is capable of binding CTLA4 from cynomolgus monkey.

130. (New) An antibody capable of binding human CTLA4, which antibody comprises:

(a) a heavy chain variable region of a human V_H 3-33 gene; and

Serial No. 09/644,668
Second Preliminary Amendment

Docket No. 4280/1M321US1
Page 11 of 17

(b) a light chain variable region of a human V_k L-15 gen .

131. (New) An antibody according to claim 130, wherein the antibody is capable of binding human CTLA4 with a binding affinity of about 10^8 M⁻¹ or greater.

132. (New) An antibody according to claim 130, wherein the antibody is capable of binding human CTLA4 with a binding affinity of about 10^9 M-1 or greater.

133. (New) An antibody according to claim 130, wherein the antibody inhibits binding of the human CTLA4 to B7-1 or to B7-2.

D
134. (New) An antibody according to claim 133, wherein the antibody reduces binding of the human CTLA4 to B7-1 by at least 50% when the concentration of antibody is at least 1 μ g/mL.

135. (New) An antibody according to claim 133, wherein the antibody reduces binding of the human CTLA4 to B7-2 by at least 50% when the concentration of antibody is at least 1 μ g/mL.

136. (New) An antibody according to claim 130, wherein the antibody does not cross-react with non-lymphoid tissue.

137. (New) An antibody according to claim 130, wherein the antibody does not bind CTLA4 from mouse.

138. (New) An antibody according to claim 130, wherein the antibody is capable of binding CTLA4 from cynomolgus monkey.

139. (New) An antibody according to claim 69 wherein the heavy chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:27, 33 and 37.

D
140. (New) An antibody according to claim 69 wherein the heavy chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:28, 34 and 38.

141. (New) An antibody according to claim 77, wherein the light chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:25, 30 and 35.

142. (New) An antibody according to claim 77, wherein the light chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:26, 31, and 36.

143. (New) An antibody according to claim 80, wherein the light chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:25, 30 and 35.

144. (New) An antibody according to claim 80, wherein the light chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:26, 31, and 36.

145. (New) An antibody according to claim 88, wherein the heavy chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:27, 33 and 37.

146. (New) An antibody according to claim 88, wherein the heavy chain variable region comprises CDR amino acid sequences set forth in SEQ ID NOS:28, 34 and 38.

147. (New) An antibody according to claim 91, wherein said antibody binds human CTLA4 with a binding affinity of about 10^9 M⁻¹ or greater.

* * * * *